The Future of Medicine starts now: How Science and New Technology are reshaping Health Science

Genoa (Italy), June 29-30, 2017

Highlights

Introduction

Prof. Frassoni and Prof. Martini, chairmen of the symposium, opened the congress, by highlighting the role played by Genomics and Genetics in Health Science. "Thanks to this congress we will be able to focus on the most important novelties in genomics related to Medicine and more in particular in physiology, diagnosis, therapy of many diseases like cancer, inflammatory diseases and also the pediatric ones", he speakers pointed out. The main topics discussed in this symposium were about genomics, epigenomics, genetics, personalized medicine, gene and target therapy and finally about genome editing. The congress has been attended by many of the top researchers of this field coming from Italy, other European and extra-European countries, together with many young physicians attending the Gaslini Institution and the University of Genoa.

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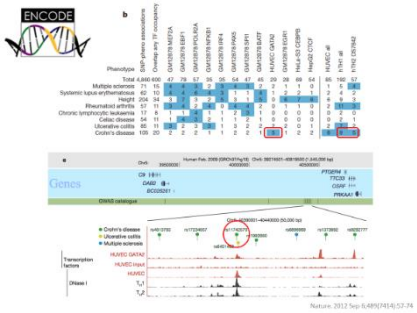
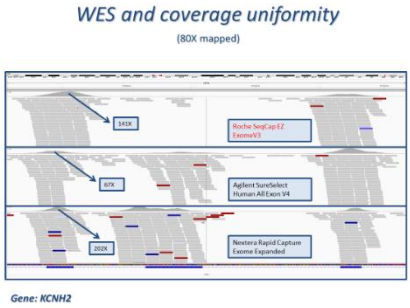
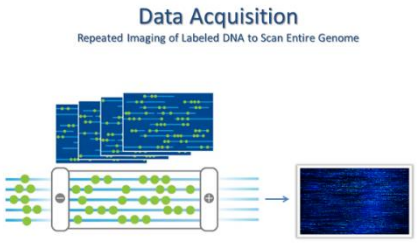
Methods, instruments and results: the relevance of governing the machinery to address the right questions



Methods, instruments and results: the relevance of governing the machinery to address the right questions, was the topic discussed by Prof. Delledonne in his lecture. The speaker, coming from Verona (it), went deeper in his talk and presented very interesting data on genetics, genomics and their main differences and integrations. In the main part of his lecture Prof. Delledonne talked about the clinical application of the whole-exome sequencing applied to clinical indications. More in particular the speaker presented very interesting data on the technological and educational issues linked with genetics and genomics. Prof. Dalledonne spoke also about three main problems, the first one characterized by the differences in sequencing technologies used by the machineries available on the market, with a significant impact on the sequencing results. The speaker talked about requesencing as the second main problem linked with the interpretation of the Variant Call format file produced by this technology. Finally, the speaker talked about the third problem characterized by the diversity in non-repetitive human sequences not found in the reference genome and presented very interesting data given by studies performed with different technologies like the Bionano ones. In conclusion, Prof. Delledonne pointed out that the beat choice for the improvement of the genomics and genetics comprehension is characterized by the application of all the different available technologies.





- Is genomics ready to help genetics to reach clinically relevant destinations?
- What's about the improvement of GWAS from the speaker point of view?
- What are the main problems related to GWAS, based on the data presented by the speaker?
- What are the main sequencing technologies presented by the speaker?
- What is the main problem linked with the VCF interpretation, based on the data presented by the speaker?
- What's about the main differences between coverage and genotyping, from the speaker point of view?
- What are the main differences between Illumina and Bionano technologies, based on the data presented by the speaker?

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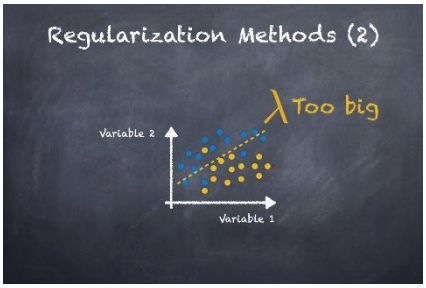
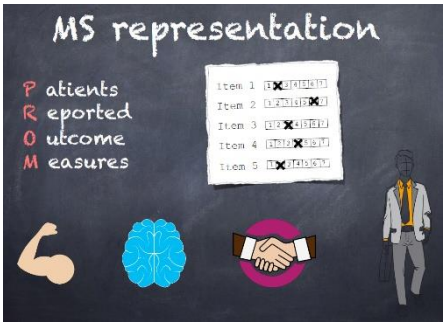
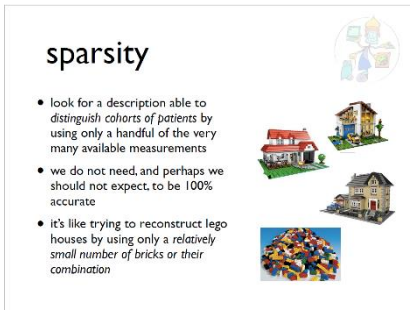
Governing the complexity of information



Prof. Verri from Genoa (IT), spoke about governing the complexity of information. The speaker talked about the data age, the successful paradigm of machine learning and the essential ingredients. Going deeper in his lecture, the speaker highlighted the problem linked with the heterogeneity of the data and pointed to the advantages linked with the advent of digital data. In the main part of his lecture, Prof. Verri, presented a very interesting model thanks to the comparison between science and machine learning. More in particular the speaker pointed out that in medicine is not necessary to find out many data, but surely many dimensions and presented very interesting data on many examples about machine learning. In the last part of his presentation, Prof. Verri talked about the application of sparsity to diagnosis, thanks to the machine learning application. In conclusion, the speaker pointed out that an Institution working on Biomedicine and Big data will be the occasion for building new medical knowledge, accelerating the development of data driven technology, and planning health care starting from quantitative analysis.





- What are the main problems linked with the heterogeneity of data from the speaker point of view?
- How can we extract information from complex data, from the speaker point of view?
- What's about artificial intelligence 2.0, based on the data presented by the speaker?
- What's about the regulation methods presented by the speaker?
- What about the application of sparsity in diagnostic medicine, based on the data presented by the speaker?

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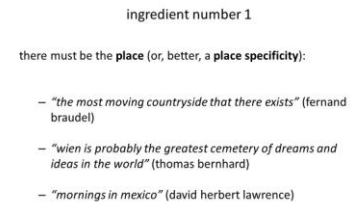
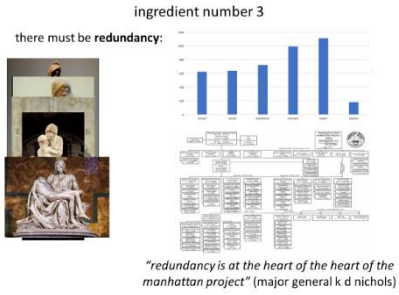
The relevance of intellectual environment for generating important research



The relevance of intellectual environment for generating important research, was the topic Prof. Piana spoke about in his lecture. The speaker coming from Genoa (IT), started his talk, by presenting very interesting data on the so called "short-circuits" between environment and knowledge. More in particular Prof. Piana talked about Michelangelo and his David, by highlighting that the committee that decided the place where definitely put the statue, was composed by the most important artists of that time and this is a very reliable example of artificial short circuits of an intellectual environment. In the second part of his lecture, Prof. Piana talked about the second and the third elements needed for the generation of a research of relevance, that are obsession and redundancy. Finally, the speaker highlighted that the fourth element is organization. In conclusion, the speaker talked about Genova and its chances to generate important research.



- What's about the International Space Science Institute, based on the data presented by the speaker?
- What's about the examples of short circuits artificially developed. Based on the data presented by the speaker?
- What's about Genoa and its possibility to generate important research, based on the data presented by the speaker?

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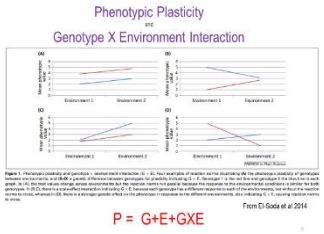
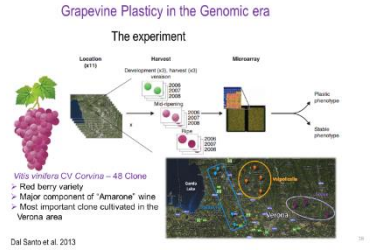
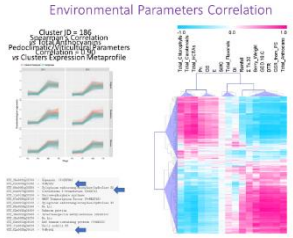
An introduction to epigenetics and DNA editing via a glass of wine



An introduction to epigenetics and DNA editing via a glass of wine, was the topic discussed by Prof. Pezzotti. The speaker, coming from Verona (IT), spoke about the phenotypic plasticity in plants and more in particular on the Grapevine plasticity from the identification to the genomic era and finally about the Grapevine genotype X environment in the genomic era. Going deeper in his lecture, Prof. Pezzotti presented very interesting data on the interaction between the phenotypic plasticity and the genotype X environment. In the main part of his lecture, the speaker talked about the meaning of the phenotypic plasticity and its use in grapevine genome sequencing. Prof. Pezzotti presented very interesting data on vintage and vineyards and the differential gene expressions due to these two elements. The speaker talked also about the transcriptome plasticity during berry development and about the correlation between plasticity, farming and environmental conditions. Finally, Prof. Pezzotti presented very interesting data on the grapevine genotyping and its correlation with environment. In conclusion, Prof. Pezzotti pointed out that his multi-year experimental design allowed to show that the variable Area has a slight impact per se on the grapevine transcriptome plasticity.





- What does plasticity mean, based on the data presented by the speaker?
- What's about the French-Italian Public Consortium for the sequencing of the Grapevine Nuclear Genome, based on the data presented by the speaker?
- What are the main questions related to the grapevine plasticity in the genomic era discussed by the speaker, based on the data presented by the speaker?
- What's about the impact of vintage and vineyards on total variability from the speaker point of view?
- What is the higher gene modulator between Sangiovese, and cabernet/Savignon grapevines, based on the data presented by the speaker?

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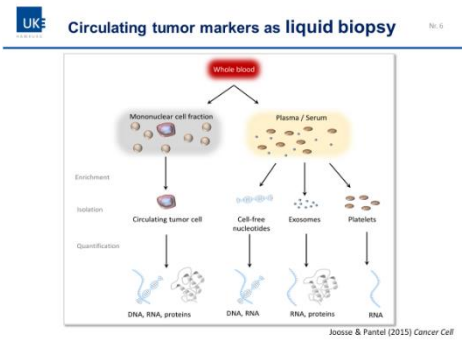
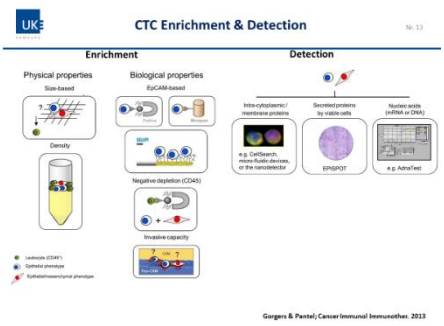
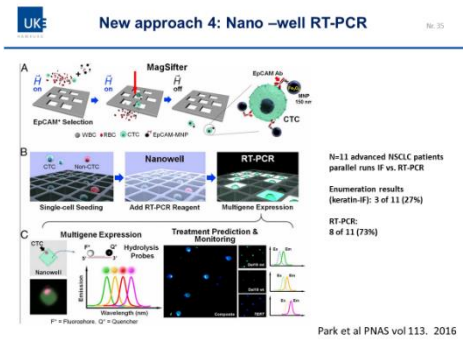
The use of circulating tumor cells (CTCs) as liquid biopsy tool in cancer research and cancer diagnostics



The use of circulating tumor cells (CTCs) as liquid biopsy tool in cancer research and cancer diagnostics, was the topic discussed by Prof. Wilkman. The speaker, coming from Hamburg (DE), talked about the metastatic cascade and the circulating tumor markers as liquid biopsy. Going deeper in her lecture, Prof. Wilkman presented very interesting data on the detection and the clinical relevance of the disseminated tumor cells in the bone marrow and on these cells as better markers of cancer heterogeneity. In the main part of her lecture, the speaker talked about the methods for the CTCs and ctDNA detection, basically divided in two steps: cell enrichment and cell detection. More in particular Prof. Wilkman presented very interesting data on the CellSearch ™ System and the role as independent predictor of survival played by CTCs in breast and metastatic cancer patients. The speaker talked also about the correlation between CTCs and Lung Cancer and presented very interesting data on the correlation between CTCs and brain metastases. In the second part of her lecture, Prof. Wilkman talked about the methods to be applied for the CTCs capture, like the in vivo and the size based ones and finally on one more technology that is the Nano-well RT-PCR. In conclusion, Prof. Wilkman pointed out that liquid biopsy holds a great promise to soon become part of the daily routine clinical diagnostic tool as a complementary assay for tissue analyses.





- When does cancer kill, based on the data presented by the speaker?
- What is the role played by the antisense lncRNAs in neurodegenerative diseases?
- Why the metastatic process is important and crucial to understand, from the speaker point of view?
- What are the main application of liquid biopsy based on the data presented by the speaker?
- What is the relationship between tissue and liquid biopsy from the speaker

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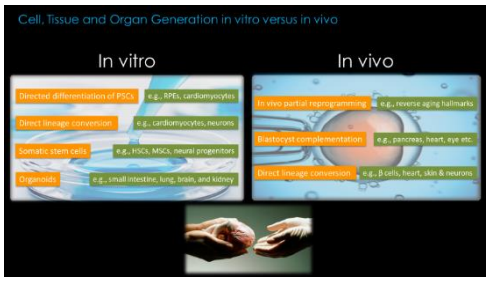
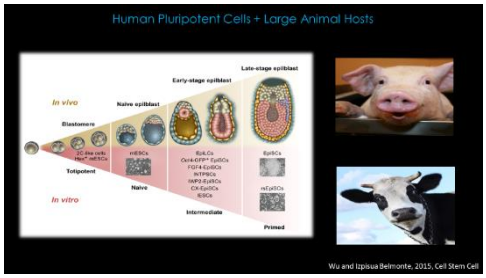
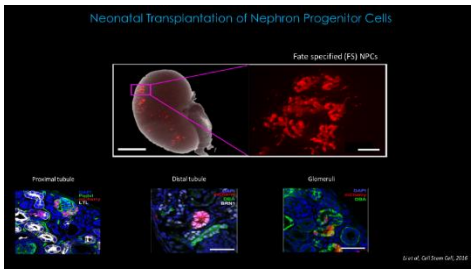
Rejuvenation vs Creation of new organs



Rejuvenation vs Creation of new organs, was the topic of Prof. Li presentation. The speaker, coming from La Jolla (USA), talked about the genetic and the epigenetic strategies and the cellular strategies. Going deeper in his lecture, Prof. Li presented very interesting data on in vitro Cell, Tissue and Organ generation compared to the in vivo ones. In the main part of his lecture, the speaker talked about the methods developed for the differentiation of potential cells, for the direct lineage conversion and for the somatic stem cells transplantation and organoids. Prof. Li presented also the main strategies developed for the in vivo tissue generation like the in vivo partial reprogramming or the blastocyst complementation and the direct lineage conversion. More in particular the speaker, talked about the interspecies chimeric processes, like chimeras between rat and mouse and highlighted that chimeras are more stable than the original animals and more useful for experiments. In the last part of his lecture, the speaker presented very interesting data on the main basic science processes, like the enhancement of donor cell chimerism or the enhancement of host permissiveness and finally on the main ethical concerns. More in particular Prof. Li talked about the possibility to develop a new kidney thanks to the neonatal transplantation of nephron progenitor cells.





- What's about the in vivo strategies developed for cells, tissue and organ generation, based on the data presented by the speaker?
- Why is it necessary to develop chimeras, based on the data presented by the speaker?
- What's about the possibility to use the interspecies chimeric complementation for the human organ generation, based on the data presented by the speaker?
- What are the key points of the neonatal transplantation of nephron progenitor cells, based on the data presented by the speaker?

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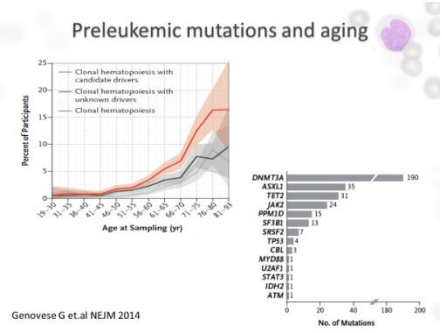
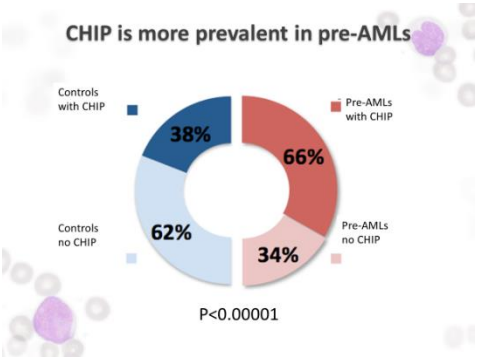
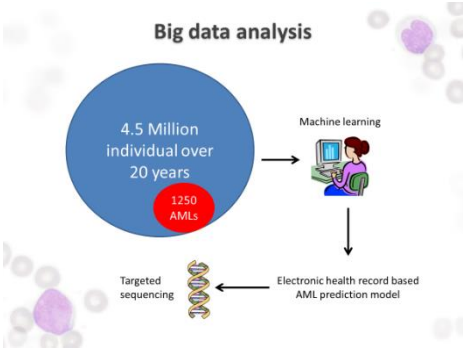
Aging, clonal hematopoiesis and preleukemia



Prof. Shlush coming from Rehovot (IL) spoke about aging, clonal hematopoiesis and preleukemia and presented very interesting data on the clonal hematopoiesis of indeterminate potential and some mutations like the TET2 ones. Going deeper in his lecture the speaker talked about preleukemic mutations and aging and presented very interesting data on the possibility to make an early diagnosis of Leukemia, thanks to the use the EIPC data, that is the European Prospective Investigation into Cancer and Nutrition study, investigating the main causes of death. In the main part of his lecture, Prof. Shlush presented very interesting data on somatic mutations and the variant allele frequency detected in Acute Myeloid Leukemia patients taking part of the EPIC study. More in particular the speaker pointed out that CHIP is more prevalent in pre-AMLs patients and also the VAF distribution is different. In the second part of his lecture, Prof. Shlush presented very interesting data on the genetic drift and more in particular on the correlation between Pre-AML somatic mutation and the older age. The speaker highlighted that the AML prediction model developed with the EPIC study has 43.2% rate of sensitivity and 99% rate of specificity more than 5 years before the diagnosis, but with low utility due to the very low prevalence of disease. Finally, Prof. Shlush talked about the future research' directions based on the EPIC results and about the potential of the big data analysis. In conclusion, the speaker pointed out that the early diagnosis and the better understanding of aging will change how we treat diseases.





- What are the main topics of the EPIC study, presented by the speaker?
- What's about the number of mutations with VAF in pre-AML patients, based on the data presented by the speaker?
- Can Leukemia be diagnosed earlier, from the speaker point of view?
- Why are the somatic mutations more frequent in older pre-AML patients, from the speaker point of view?
- What's about the genetic drift presented by the speaker?

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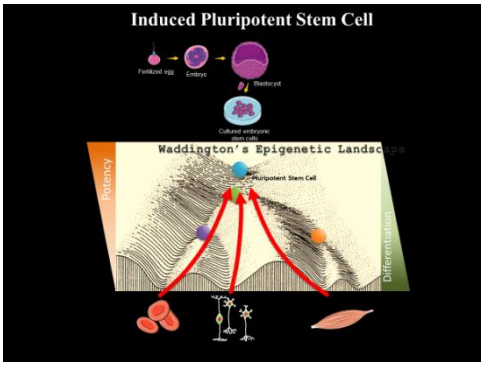
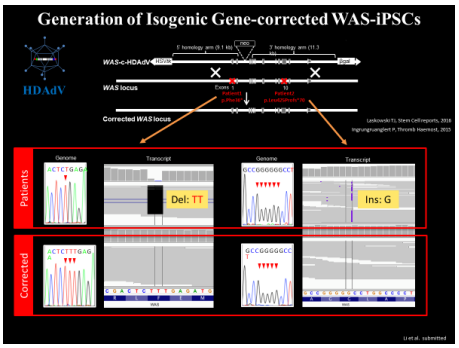
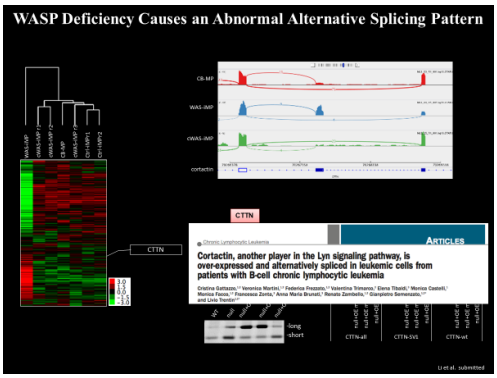
Perspectives of single cell genome analysis



Prof. Li from Kaust (SA), spoke about perspectives of single cell genome analysis and presented very interesting data starting from a good disease model definition. Going deeper in his lecture, Prof. Li pointed out that the pluripotent stem cells can be the right model for a disease definition. In the main part of his lecture, the speaker presented very interesting data on the iPSC model for genetic diseases thanks to the application of the genome sequencing technology and talked about the application of this model for the diagnosis of the Wiskott-Aldrich Syndrome. More in particular Prof. Li presented very interesting data on the WASP gene, its main mutations and the relationship between genotype and phenotype. The speaker presented also very impressive data on the possibility to repair the mutations through the generation of isogenic gene-corrected WAS-iPSCs. Prof. Li talked also about other experiments involving hematopoietic cells differentiated from WAS-iPSCs, able to recapitulate well-known disease phenotypes. Finally, the speaker presented very interesting data on the possibility to reveal novel functions of WASP in the nuclear body formation through the WASP iPSC model application.





- What is a good disease model from the speaker point of view?
- What are the main characteristics of the Wiskott-Aldrich Syndrome presented by the speaker?
- What are the main functions of the WASP gene in the immune cells. Based on the data presented by the speaker?
- What is the effect of mutant WASP on the nuclear speckles in B cells, based on the data presented by the speaker?
- What is the nuclear localization of WASP in blood cells, based on the data presented by the speaker?

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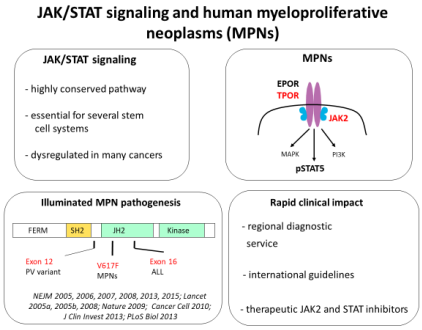
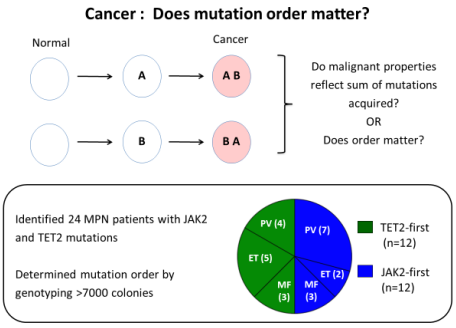
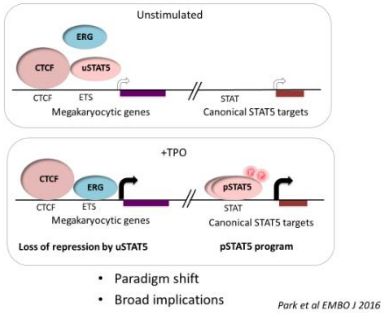
The effect of mutation order in Neoplasias



Prof. Green from Cambridge (USA), spoke about the effect of mutation order in Neoplasias. More in particular, the speaker talked about the myeloproliferative neoplasms and about the JAK/STAT signaling in MPNs. Going deeper in his lecture, Prof. Green presented very interesting data on the phenotypic driver mutations and on their order. In the main part of his lecture, the speaker presented very interesting data on the effects that mutation order determines on the clonal evolution and on the possible mechanisms. More in particular Prof. Green spoke about the two possible mechanisms of the mutation order able to influence the clonal evolution and presented very interesting data on the clonal analysis of altered cells and on the cytokine signalling driven by tyrosine unphosphorylated STATs. Speaking about mutation order, Prof. Green highlighted that not only the order directly influences the clonal evolution, but also the response to therapy and it was demonstrated in any type of cancer. In the last part of his lecture, the speaker presented very interesting data on the cytokine signalling and more in particular on the interaction between cytokines and pSTAT5 at the tissue level. In conclusion, Prof. Green pointed out that his data provide paradigm shift in understanding of cytokine signalling through the JAK/STAT pathway and rise many implications for normal tissues, multiple malignancies and STAT inhibitors.





- **Does the mutation order matter in cancer, based on the data presented by the speaker?**
- **What are the main topics of the mutation order mechanism presented by the speaker?**
- **What is the biological significance of the different transcriptional responses to JAK2 mutation, based on the data presented by the speaker?**
- **What's about the integration between cytokines and the tissue networks, based on the data presented by the speaker?**
- **What's about the role played by STAT5 in the integration of the cytokine signalling at the tissue level, based on the data presented by the speaker?**

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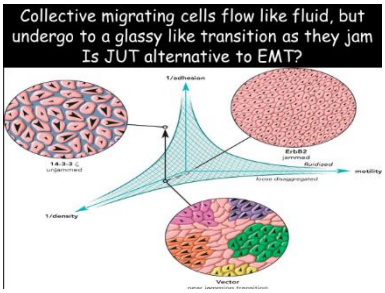
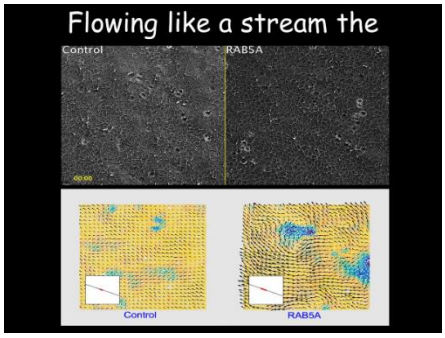
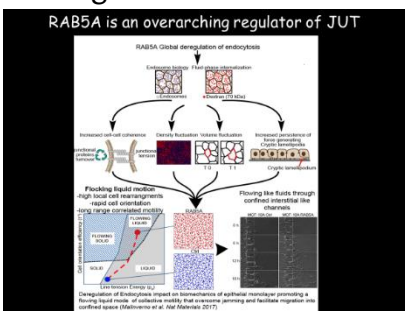
The natural history of metastases and the similarities and differences between “liquid” and “solid” tumors



The natural history of metastases and the similarities and differences between “liquid” and “solid” tumors, was the topic discussed by Prof. Scita from Milan (IT), more in particular the speaker talked about cell movements finalized to life, development, repair and finally about the migration in cancer and metastasis. Going deeper in his lecture, Prof. Scita presented very interesting data on the pathway of migration of cancer and metastatic cells. In the main part of his presentation, the speaker talked about the multistep process leading to the dissemination of the metastatic cells starting from the primary tumor. More in particular Prof. Scita presented very interesting data on the multiple mode of migration and their specific pathways. The speaker talked also about the two main modalities used for migration, like flowing and moving like bullets and presented very interesting data on the transition phase between solid and liquid.





- What is the underline motility machinery leading to the cells different movements, based on the data presented by the speaker?
- What are the different forms and shapes of the collective locomotion, based on the data presented by the speaker?
- What’s about the different types of cluster locomotion, based on the data presented by the speaker?
- What’s about the main multiple mode of migration, based on the data presented by the speaker?
- What are the molecular bases of endocytosis-mediated biomechanical unjamming of solid-like collective epithelial, based on the data presented by the speaker?

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Clinical trials in pediatric rheumatic disease

Prof. Martini from Genoa (IT), presented very interesting data on clinical trials in pediatric rheumatic disease. More in particular the speaker talked about the difficulties in performing controlled trial in children. Going deeper in his lecture, the speaker pointed out that children are not little adults and there is the need for the development of drugs specifically designed for them. In the main part of his talk, Prof. Martini presented very interesting data on the FDA and EMA rules for pediatric studies and more in particular he spoke about the PRINTO network. Prof. Martini presented also very interesting data on the main clinical trials running in pediatric patients affected by juvenile idiopathic arthritis performed by the PRINTO network. In the second part of his lecture, the speaker talked about the drug development and the role played by PRINTO in this process, together with industry. More in particular Prof. Martini presented also the main not-for-profit PRINTO trials running in paediatrics thanks to the founding of Industry. In the last part of his lecture, the speaker talked about some issues like the need to test the combination therapy in JIA patients for the lack of data in these patients. Prof. Martini discussed also other topics like biosimilars and me-too drugs applied in pediatric diseases or the need for rethinking JIA classification and nomenclature. The speaker talked also about another problem related to the survival of the pediatric rule due to the difficulty to enrol enough patients for clinical trials in many pediatric diseases. In conclusion, Prof. Martini pointed out that there is the need for establishing a strong link between regulatory authorities and academia.

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- What are the countries taking part of the PRINTO network?
- How many clinical trials have been performed by PRINTO in JIA, based on the data presented by the speaker?
- What's about the role played by PRINTO in the drug development process from the speaker point of view?
- What's about the standard of care PRINTO JDM trial presented by the speaker?
- What are the main characteristics of the pediatric-rheumatology.pinto.it site presented by the speaker?

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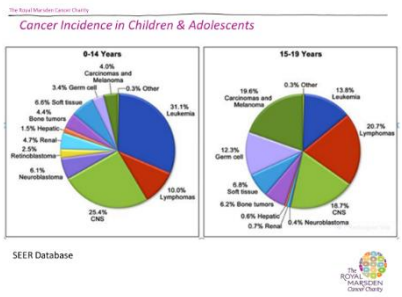
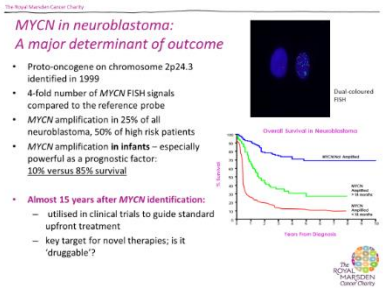
How to develop clinical trials in the new era of Medicine



"How to develop clinical trials in the new era of Medicine" was the topic of Prof. Marshall presentation. The speaker, coming from London (UK), presented very interesting data on childhood cancers, by highlighting that cancer is fortunately rare in childhood but it is the most common cause of death under 15 years, more in particular in the developed countries. Going deeper in her lecture, Prof. Marshall pointed out that the high-risk groups remain poor prognosis despite the toxic therapy and this is the case of neuroblastoma, metastatic sarcoma, leukemia and relapsed lymphoma. In the main part of her lecture, the speaker presented very interesting data on the pediatric process of drug development and spoke about the pediatric regulation and the pediatric investigational plan. Prof. Marshall talked also about personalized cancer therapy applied to pediatrics and adolescents and highlighted the importance of the multi-stake-holder interaction in pediatric oncology. The speaker talked also about the International/European landscape of pediatric early phase trials, that is a network involving 51 centers across 12 countries and presented very interesting data on the objectives and the key strategies in phase I and II trials in pediatrics. In the second part of her lecture, the speaker talked about the mutational burden of the pediatric tumors and presented very interesting and impressive data on the major mutations typical of the high-grade gliomas and neuroblastomas. Speaking about neuroblastoma, Prof. Marshall presented very impressive data on the standard treatment and on immunotherapy, thanks to the data of the BEACON-Neuroblastoma european study. Finally, the speaker talked about the european Precision Medicine Program in pediatric hemato-oncology and presented very interesting data on E SMART that is the European proof of concept therapeutic stratification trial of molecular anomalies in relapsed or refractory tumors in children. In conclusion, the speaker pointed out that parents and patients want and need novel therapies.



- What is the cancer incidence in children and adolescents, based on the data presented by the speaker?
- What are the main bottlenecks in the cancer drug development for pediatric patients, based on the data presented by the speaker?
- What are the countries taking part of the Innovative therapies in Children with cancer association?
- What's about the MYCN amplification for the neuroblastoma prognosis, based on the data presented by the speaker?
- What are the main topics of the E-SMART project presented by the speaker?

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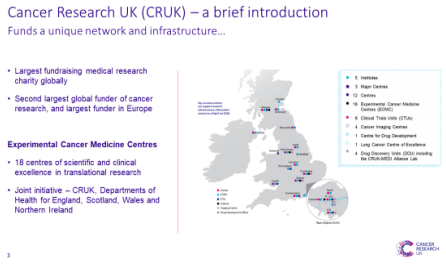
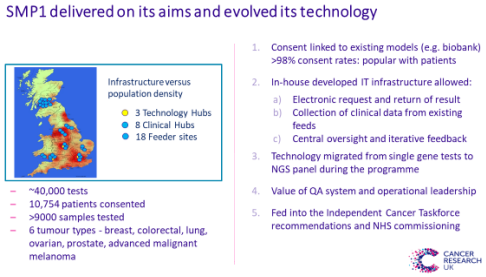
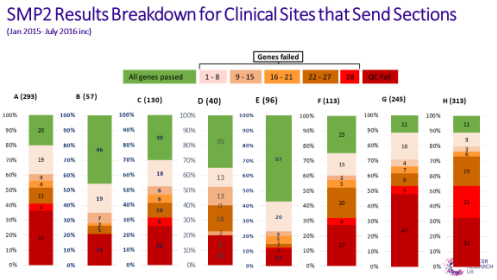
How UK is tackling the challenge of implementing Precision Medicine



The main topic of Prof. Subramaniam presentation, was "How UK is tackling the challenge of implementing Precision Medicine". The speaker, coming from London (UK), presented very interesting data on the cancer research in UK, the precision medicine and the early challenges and finally on the stratified medicine programme. Going deeper in her lecture, Prof. Subramaniam talked about the network and the infrastructure of the Cancer Research UK aiming to the development of the precision medicine project, based on the need to stratify patients on the basis of the genomic analyses. In the main part of her lecture, Prof. Subramaniam presented very interesting data on the stratified medicine programme part 1 aiming to understand the requirements and the challenges associated with a national wide system for molecular testing in cancer. The speaker talked also about the part 2 of this project aiming to the screening for lung cancers for clinically relevant molecular signals. More in particular Prof. Subramaniam pointed out that SMP2 works within current NHS pathology pathways in order to deliver high quality, targeted sequencing and presented the main steps which characterize this project. In the second part of her talk, the speaker presented very interesting data on the MATRIX study that is an umbrella genetic study running in lung cancer patients. In conclusion, Prof. Subramaniam pointed out that it is necessary to continue to learn in this ever changing, complex landscape, with the knowledge that information about the tumour DNA can help to treat patients in a more precision way.





- **What are the key topic of the Stratified Medicine Programme part 1 and 2 presented by the speaker?**
- **Why is the part 2 SMP program dedicated to the screening of lung cancers, based on the data presented by the speaker?**
- **What are the main topics of the National Lung MATRIX trial, presented by the speaker?**
- **What's about the SMP2 patient attrition, based on the data presented by the speaker?**

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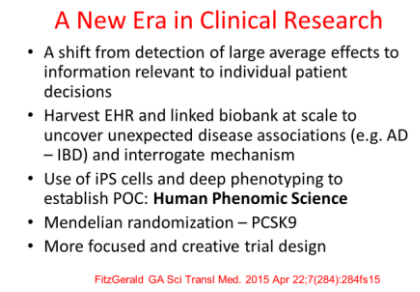
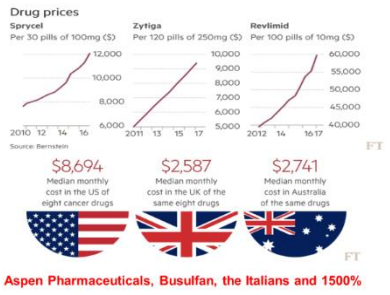
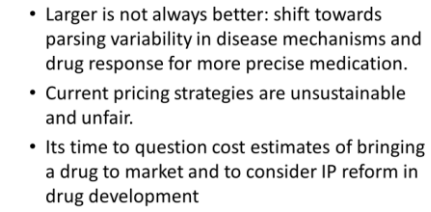
Future perspectives in translational medicine



Prof. Fitzgerald from Philadelphia (USA), spoke about future perspectives in translational medicine and presented very interesting data starting from the new drugs approved by FDA in the last year. Going deeper in his lecture, Prof. Fitzgerald talked about the study rate per phase, and highlighted that there are 10 % of probabilities that a new drug starting from the early phases can come into market. In the main part of his lecture, the speaker presented very interesting data on the Institute for Translational Medicine and Therapeutics (ITMAT) and its mission. More in particular Prof. Fitzgerald talked about the main topics of what he addressed as the new era in clinical research and presented very interesting data on the new challenges in clinical research characterizing our times, like how to predict resistance of the PD-1 blockade, or how to approach combinatorial strategies also with drugs in development. In the second part of his lecture, Prof. Fitzgerald talked about Pricing and Innovation starting from the gene therapy example, where despite very poor results, the costs of the new drugs raised in a quite unsustainable way. The speaker presented also very impressive data on the Political and Scientist reaction to this phenomenon. Finally, Prof. fitzgerald presented very interesting data on new models for IP. In conclusion, the speaker pointed out that to consider IP reform in drug development.





- What are the key points of the ITMAT mission, based on the data presented by the speaker?
- What are the main factors of the New Era in clinical Trials, based on the data presented by the speaker?
- How precisely Translational Science does delivery, based on the data presented by the speaker?
- What's about the true cost of drugs in USA, based on the data presented by the speaker?
- How do we foster innovation while containing cost and spreading benefit, based on the data presented by the speaker?

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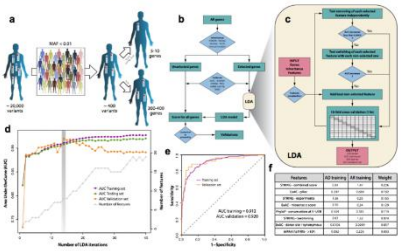
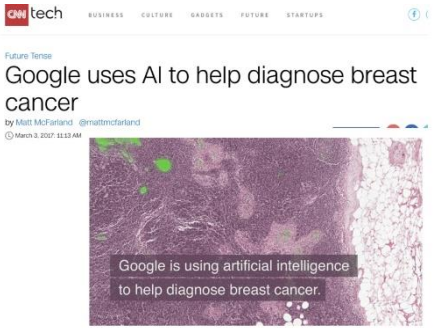
Informatics, bioinformatics and genetic disorders

The DOMINO project: an algorithm to estimate the likelihood for a gene to arbor dominant mutations



Informatics, bioinformatics and genetic disorders, was the topic discussed by Prof. Furga from Lausanne (CH). More in particular the speaker presented very interesting data on the next generation sequencing, pointing to the dramatic increase in the number of genetic disorders thanks to NGS. In the main part of his presentation, Prof. Furga, talked about the DOMINO project, that is an algorithm able to estimate the likelihood for a gene to arbor dominant mutations. The speaker presented also the main characteristics and the results of the DOMINO project, by highlighting that the results are quite good. In the second part of his presentation, the speaker talked about machine learning and artificial intelligence (AI), starting from the way they work and presented very impressive data given by a study on the use of google as a diagnostic tool and another study on the screening for pancreatic cancer using signals from web search logs. Speaking about artificial intelligence, Prof. Furga presented very impressive data on the AI application for diagnosis, by highlighting that physicians have to learn from AI. In conclusion, Prof. Furga pointed out that if physicians do not use AI, they will stay behind and not serve their patients.



"Geometry" - Handling visual information

- What are the key topics of the DOMINO project presented by the speaker?
- What are the main results of the DOMINO project, based on the data presented by the speaker?
- Can a computer be trained to make sense of clinical data, based on the data presented by the speaker?
- What's about the "deep neural network" training set, based on the data presented by the speaker?
- How can AI replace clinical diagnosis by a physician, based on the data presented by the speaker?

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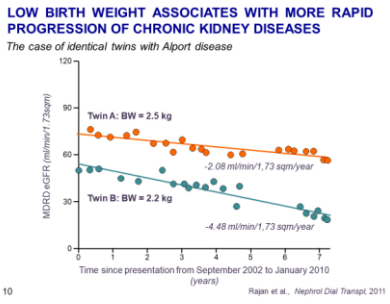
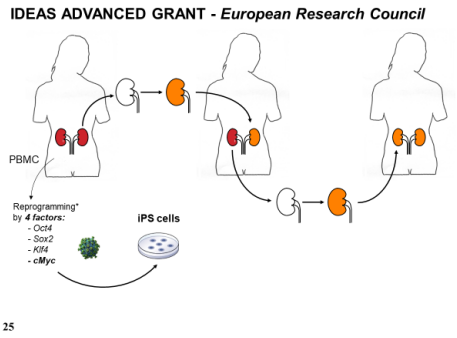
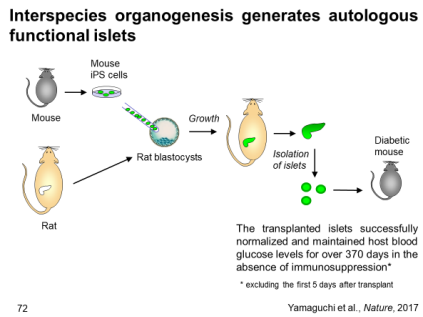
Nephrology: a glance over the future



Prof. Remuzzi from Bergamo (IT), spoke about Nephrology: a glance over the future. More in particular, the speaker talked about the global burden of disease. Going deeper in his lecture Prof. Remuzzi, presented very interesting data on the "future" nephrology, by highlighting that the renal diseases start from the in-utero life. In the main part of his lecture, the speaker presented very impressive data on the relationship between birth weight and the progression of chronic kidney disease and spoke about a clinical study running in pre-born babies for an in vivo quantification of the placental insufficiency by BOLD MRI. Prof. Remuzzi, presented also very interesting and impressive data on the renal transplantation results together with the effects of the new immunosuppressive drugs. In the second part of his lecture, the speaker talked about another issue like the lack of donor organs and the need for the creation of organs and presented very interesting data on the solution, through the reprogramming of IP cells. Prof. Remuzzi presented also other data given by studies on the kidney regeneration thanks to engineering processes, by highlighting that this is the future of nephrology not the present. Finally, the speaker spoke about an alternative use of cells' inherent abilities to organize themselves in order to make possible the transplantation of an organoid kidney and presented very impressive data on experiments running in human cells for the development of neo-nephrons and the generation of podocytes and spoke about blastocytes manipulation. In conclusion, Prof. Remuzzi pointed out that this is the way for the future but we have to be very careful in order to avoid the same result of the flight of Icarus.





- How many nephrons are developed within the third month of pregnancy, based on the data presented by the speaker?
- What's about the global challenges for low-weight babies born in low and middle-income countries, based on the data presented by the speaker?
- What are the key topics of the IDEAS project presented by the speaker?
- What does organoid mean, based on the data presented by the speaker?
- What's about the creation of human organs in pigs from the speaker point of view?

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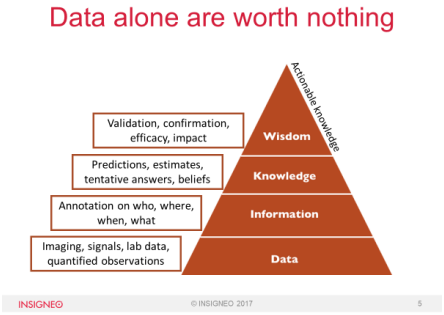
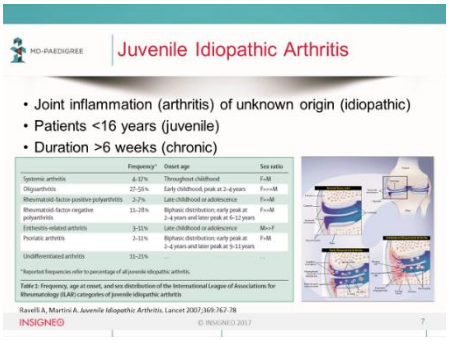
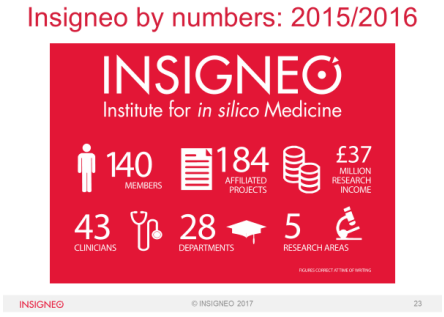
Big Data analysis and virtual physiological human



Big Data analysis and virtual physiological human, was the topic discussed by Prof. Viceconti from Shieffield (UK), more in particular the speaker talked about the meaning of the data per sè, by highlighting that data alone are worth nothing, Going deeper in his lecture, Prof. Viceconti presented very interesting data on the virtual physiological human (VPH) as the way for a predictive medicine where the all patients data are analysed by specialised model that provide support to medical decision. In the main part of his lecture, the speaker talked about the data related to the JIA project and the research hypotheses. More in particular Prof. Viceconti presented very impressive data on the methods used for the subject-specific model, the second specific model, their validation and the main results obtained. In the second part of his lecture, the speaker talked about INSIGNEO that is the Institution for silico in Medicine and its main activities in human projects. In conclusion, Prof. Viceconti, pointed out that the mere accumulation of data will not automatically improve healthcare, but for transforming data into actionable knowledge the most effective approach is to combine data and prior knowledge and subjects-specific models open a predictive medicine scenario, starting from clinical studies.





- What are the main results of the JIA project presented by the speaker?
- What's about the biomarkers' overview, based on the data presented by the speaker?
- What's about the joints kinematics and movements, based on the data presented by the speaker?
- What's about the individual load reduction strategy and its influence on the response to therapy, based on the data presented by the speaker?
- What are the main projects planned by INSIGNEO, presented by the speaker?

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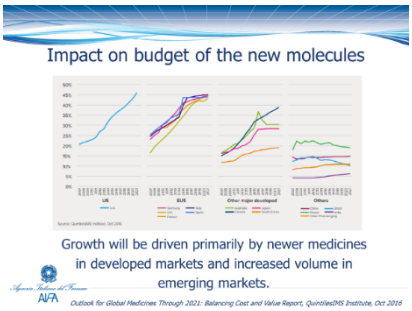
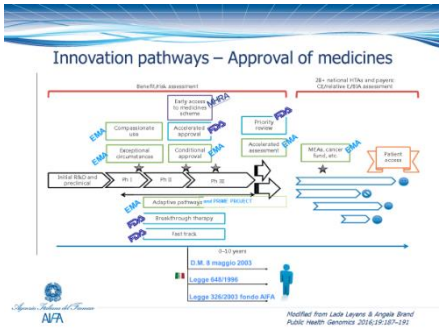
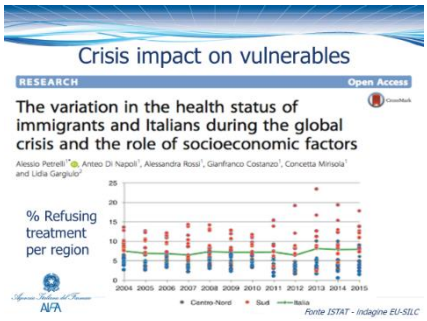
New challenges for Regulatory agencies



Prof. Erba from Rome (IT), presented very interesting data on New challenges for Regulatory agencies. More in particular the speaker talked about the mission of the Italian Agency of Medicines. Going deeper in his lecture, Prof. Erba presented very impressive data on the chronic diseases and the pharmaceutical expenditure from 1985 to 2016 in Italy. In the main part of his lecture, the speaker talked about the new challenges and, more in particular he presented very interesting data on the sustainable innovation characterized by three fundamental domains like the clinical needs, added therapeutic value and quality of evidence. Prof. Erba talked also about the role of AIFA in enhancing innovation and in improving the access to cure and presented very interesting data on the method used for defying the price of the drugs. In the second part of his presentation, the speaker talked about equity, the disruptive medical technologies, like CAR T cell production and gene therapy, by highlighting that today Regulators are not ready. Finally, Prof. Erba talked about the global complexity and presented very interesting data on ICMRA that is the International Coalition of Medicines Regulatory Authorities, aiming to support communication and address regulatory science issues. In conclusion, Prof. Erba pointed out that AIFA is committed to grant every patient the most appropriate therapy based on scientific evidence and validated data.





- What is the impact on budget of the new molecules, based on the data presented by the speaker?
- What 's about the regional dishomogeneity, based on the data presented by the speaker?
- What are the AIFA criteria for the Innovation evaluation, based on the data presented by the speaker?
- What is the role of AIFA in enhancing innovation and in improving access to cure, based on the data presented by the speaker?
- How to define the price of drugs, based on the data presented by the speaker?
- What's about the variation in the health status of immigrants and Italians during the global crisis, based on the data presented by the speaker?
- How to produce the CAR T cells, based on the data presented by the speaker?

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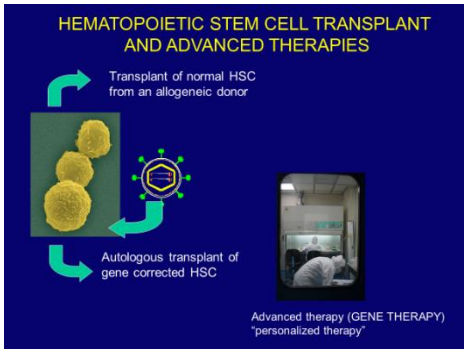
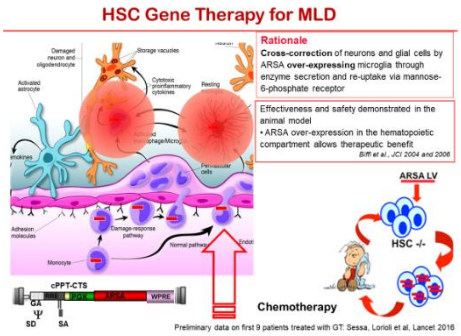
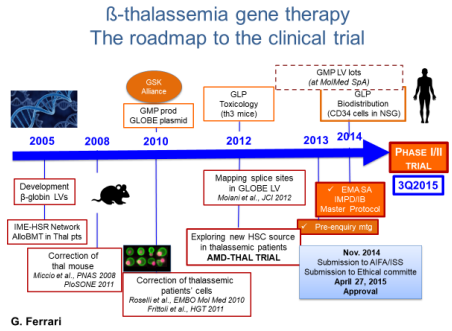
Gene therapy



Prof. Aiuti from Milan (IT), spoke about gene therapy and presented very interesting data starting from the gene therapy platform characterized by gene addition with integrating vectors, gene editing and disruption and finally by gene addition with inhibitory activity. Going deeper in his lecture, Prof. Aiuti talked about the Gene therapy approach for genetic diseases starting from the ex-vivo processes to the in-vivo ones. In the main part of his lecture, the speaker presented very interesting data on the scientific challenges related to the gene therapies of the rare diseases. More in particular Prof. Aiuti talked about the hematopoietic stem cells transplantation (HSC) and the advanced therapies and presented very interesting data on the ex vivo HSC gene therapy for genetic diseases given by clinical studies running in pediatric patients affected by ADA-SCID that is a very rare genetic disease, characterized by a total recovery after ex-vivo gene therapy. Prof. Aiuti presented other very interesting data on the gene therapy applied to patients affected by the Wiskott-Aldrich syndrome, given by a Phase I and II clinical trial running in these patients. The speaker talked also about gene therapy applied in other pediatric genetic syndromes like metachromatic leukodystrophy and β-thalassemia.





- What are the main challenges of the gene therapies for the rare diseases, based on the data presented by the speaker?
- What's about autologous gene modified HSC transplantation, from the speaker point of view?
- What are the main advantages of the HSC gene therapy, based on the data presented by the speaker?
- What's about the role of HSC source and the preparatory regimen, based on the data presented by the speaker?
- What's about ADA-SCID gene therapy, based on the data presented by the speaker?
- What's about the WAS Lentiviral gene therapy, based on the data presented by the speaker?
- What are the main effects of gene therapy in MLD patients, based on the data presented by the speaker?

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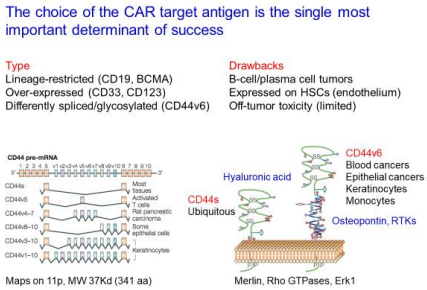
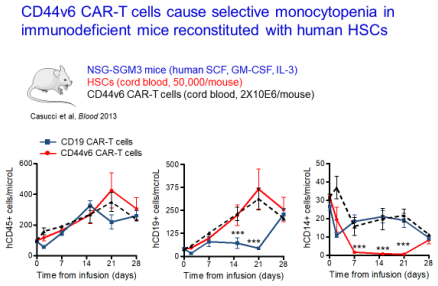
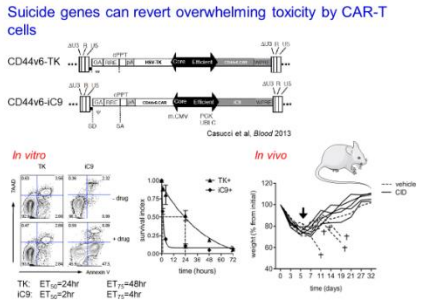
CAR-T for cancer autoimmune and inflammatory diseases



CAR-T for cancer autoimmune and inflammatory diseases, was the topic discussed by Prof. Bondanza from Milan (IT), more in particular the speaker presented very interesting data on the concept that immune checkpoint blockade and engineering T cells are two radically different approaches to cancer immunotherapy. Going deeper in his lecture, the speaker presented very interesting data on CAR-T cells characteristics from the engineering and the pharmacological point of view. In the main part of his lecture, Prof. Bondanza talked about the major unmet needs related to these T cells and presented very interesting and impressive data on the CAR-T cells effects in many tumors. From the pharmacokinetic point of view the speaker talked about the CRR-T cells manufacturing with CD3/CD28 beads and highlighted that these processes have ameliorated their efficacy. Prof. Bondanza presented also very interesting data given by a clinical study running on patients affected by leukemia, where the modified CAR-T cells have provided both short and long-term disease control. Finally, the speaker talked also about toxicity and presented very interesting and impressive data, demonstrating that CD44v& CAR-T cells cause a very selective monocytopenia and that Keratinocytes are naturally protected from these modified cells. In conclusion, Prof. Bondanza pointed out that CD44v6 CAR-T cells are new players in the AML syndrome with a different profile.





- What are the major unmet needs in the field of CA-T cells, from the speaker point of view?
- What are the main effects of the CD44 CAR-T cells, based on the data presented by the speaker?
- What's about Keratinocytes and CAR-T cells based on the data presented by the speaker?
- What's about the relationship between CR-T cells adverse events and Tocilizumab/Anakinra, based on the data presented by the speaker?

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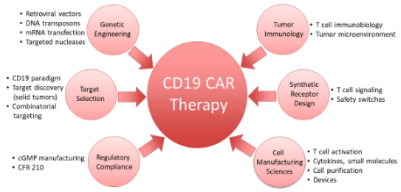
Chimeric antigen receptors: driving immunology towards synthetic biology

Assembling CARs for T Cell Therapy



Rivière & Sadelain, *Mol Ther*, 2017

Prof. Sadelain from New York (USA), spoke about chimeric antigen receptors: driving immunology towards synthetic biology and presented very interesting data starting from the concept that engineered T cells may combine specific, potency and persistence in a single optimized "living drug". Going deeper in his lecture, the speaker presented very interesting data on CD 19 CAR therapy effects in systemic B cell malignancies in mice. In the main part of his lecture, Prof. Sadelain presented very interesting data on the effects of CAR T cell treatment on the overall survival in adult patients affected by acute lymphatic leukemia and on safety. More in particular the speaker talked about the goals and strategies of the therapeutic T cell design, characterized by the auto co-stimulation and the delayed exhaustion. In the second part of his talk, Prof. Sadelain presented very interesting data on the genetic engineering evolution, mainly characterized by the CRISP/Cas9-targeted integration into the TRAC locus leading to a higher homogenous car expression in TRAC-CAR T cells. Finally, the speaker talked about the main diseases responding to CAR therapy.

Cytokine release syndrome (CRS) & neurological toxicities

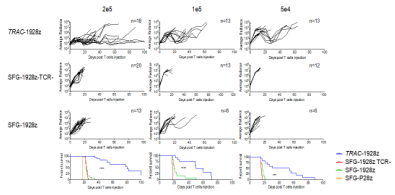
- Cytokine release syndrome (CRS)
  - Fever
  - Hypotension
  - Respiratory insufficiency
- Neurological changes
  - Delirium
  - Aphasia
  - Global encephalopathy
  - Seizure-like activities/seizure

	Morphologic Disease (N=31) [95% CI]	**Minimal Disease (N=20)** [95% CI]
Severe CRS	13 (42%) [25 – 61]	1 (5%) [0 – 25]
Grade 3/4 Neuro Toxicities	18 (58%) [39 – 75]	3 (15%) [3 – 38]
Grade 5 Toxicity	3 (13%)¶	0

¶All pts received a higher dose ($3x10^6$ CAR T cells/kg): 2 pts with sepsis and 1 pt with CRS.

- No grade 5 neurotoxicity has been observed.
- No case of cerebral edema has been observed.
- Use of Tocilizumab and/or steroids did not impact EFS or OS

TRAC-CAR T cells vastly outperform conventional CAR T cells *in vivo*



Eyquem, Mansilla-Soto et al, *Nature*, 2017

- What is the CAR T cell manufacturing flow presented by the speaker?
- What's about the correlation between the Cytokine release syndrome and the CAR-T cell therapy, based on the data presented by the speaker?
- What's about TRAC-CAR T cells performance, based on the data presented by the speaker?
- What is the TRAC-CAR model presented by the speaker?
- What are the main diseases treated with CAR-T cell therapy, based on the data presented by the speaker?

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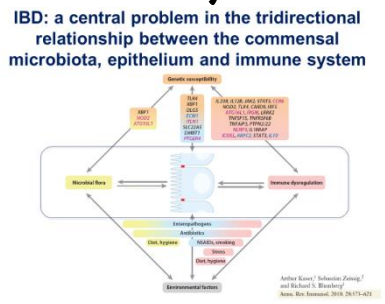
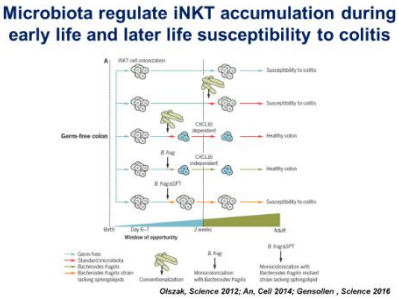
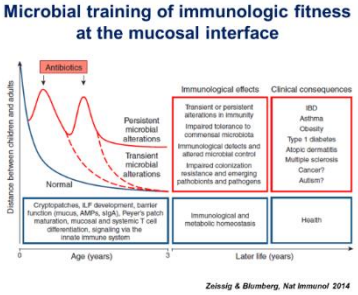
How colonisation by microbiota in early life shapes the immune system



How colonisation by microbiota in early life shapes the immune system was the topic discusses by Prof. Blumberg. The speaker coming from Boston (USA), presented very interesting data on Inflammatory Bowel Disease as a central problem in the tridirectional relationship between microbiota, epithelium and immune system. Going deeper in his lecture, Prof. Blumberg pointed out that IBD has an increasing incidence and prevalence around the world more in particular in the first decade of life. In the main part of his talk, the speaker presented very impressive data, showing that the change of the environment is the most important cause of this epidemics. More in particular the speaker talked about the mendelian transmission of this disease as a monogenic disorder and discussed many data published in some papers on the protective microbial factors against the onset of IBD. Prof. Blumberg presented also very interesting and impressive data on the NKT cells, the so called invariant natural killer T cells, involved in other inflammatory human diseases like ulcerative colitis and their relationship with microbiota particularly in the early life. The speaker presented a lot of very interesting data given by animal studies, demonstrating that a germ-free colon is rapidly colonized by the iNKT cells and it is more susceptible to colitis. In the second part of his presentation, Prof. Blumberg talked about the correlation between asthma, eczema, hay fever and iNKT cells and demonstrated that this relationship is modulated by the microbiota. In the last part of his lecture, Prof. Blumberg presented very interesting data on the phylogenetic microbiota composition, by highlighting that in people living in high-income countries the microbiota does not increase in diversity as it does in other people living in low-income countries and presented very interesting data on the correlation between a long exposure to antibiotics in the first years of life and the onset of IBD, asthma, obesity diabetes and other diseases later on in the life.





- What are the main genetic characteristics of IBD as monogenic disease, based on the data presented by the speaker?
- What are the main topics linked with the IBD hygiene hypothesis presented by the speaker?
- What's about the relationship between iKNT cells and microbiota, based on the data presented by the speaker?
- What's about the relationship between asthma, eczema, hay fever and iNKT cells, based on the data presented by the speaker?
- What's about the differences in microbiota between USA people and other people living in low-income countries?

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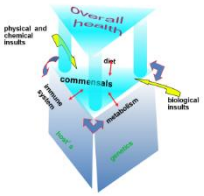
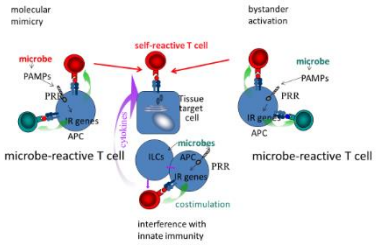
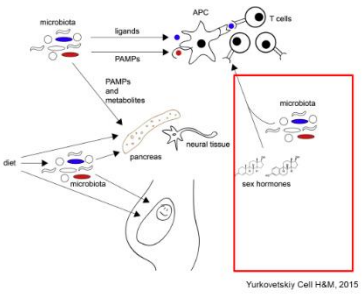
Microbiota and autoimmunity



Prof. Chervonsky from Chicago (USA), spoke about microbiota and autoimmunity and presented very interesting data starting from the consideration that genetic is important for diseases, but environment plays a very important role. Going deeper in his lecture, the speaker talked about the confounding factors related to the interactions between host and his microbiota and presented very interesting data on the Omics cascade. In the main part of his lecture, Prof. Chervonsky presented very interesting data on the germ-free animal experiments demonstrating the influence of microbiota in different types of immunity. More in particular the speaker talked about the relationship between microbiota and diseases that develop independently of commensals like type 1 diabetes in mice and rats, where the microbiota different bacterial composition can affect the onset of the disease. Prof. Chervonsky presented also very interesting data on the association between microbiota and disease, more in particular on the ways microbes interfere with the innate and the adaptive autoimmune response: the modification of the innate responses, molecular mimicry and bystander activation. The speaker, talked also about the correlation between microbiota, autoimmunity and sex and about the correlation between microbiota, diet and autoimmunity. Finally, Prof. Chervonsky presented very interesting data on the effects of a gluten enriched diet on the immune system through the involvement of the microbiota. In conclusion, the speaker pointed out that the definition of signaling pathways regulated or co-regulated by the microbiota, would advance our understanding and treatment of the autoimmune diseases.





- Why there is the need for experimental systems for biological validation of OMICS findings?
- How microbes can interfere with autoimmunity?
- What's about molecular mimicry, based on the data presented by the speaker?
- What's about the correlation between microbiota, autoimmunity and sex, based on the data presented by the speaker?
- Are there processes that can be influenced in microbiota-independent manner, from the speaker point of view?
- What is the effect of a glute enriched diet on autoimmunity, based on the data presented by the speaker?

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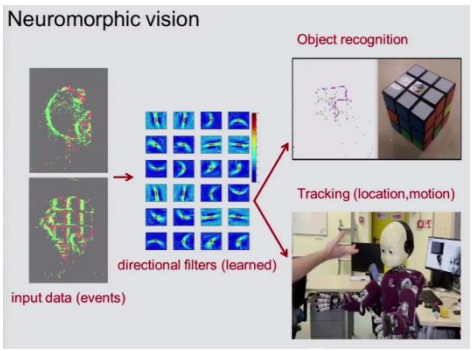
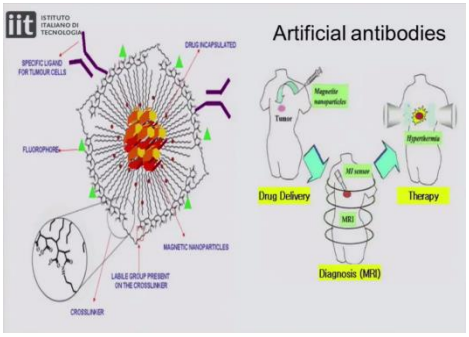
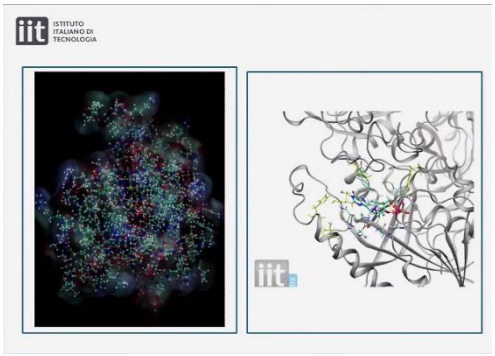
Frontiers of nanotechnology for health



Frontiers of nanotechnology for health was the topic discussed by Prof. Cingolani. The speaker coming from Genoa (IT), presented very interesting data on the rehabilitation through humanoids, the robotic surgery, the vision, the multifunctional drug delivery, the point of care diagnostics and finally on the high-performance computing. Going deeper in his lecture, the speaker talked about humanoids and presented very interesting data on their application in diagnosis and in the rehabilitation procedures. More in particular Prof. Cingolani spoke about a robot able to read the specific code bar of any drug and then distribute them to patients and also about the interaction between autistic children and humanoids. In the main part of his lecture, the speaker presented very interesting data on the applications of the robot surgery, more in particular in the endoscopes field. Prof. Cingolani talked also about vision, by highlighting the role of the neuromorphic vision and the implantable artificial retina. In the second part of his lecture, the speaker presented very interesting data on the multifunctional drug delivery and spoke about the methods of drug release directly at the site of the targeted lesion. Finally, Prof. Cingolani presented very interesting data on the application of the nanotechnology in diagnostics like food degradation and spoke about the high performance technology and its application in pharmacology for the design of new drugs.





- What's about the material composing the robot presented by the speaker?
- How many robots like the one presented by the speaker will be at work in the future from the speaker point of view?
- What's about the interaction between autistic children and humanoids, based on the data presented by the speaker?
- What's about the precision of the endoscope developed for the robot surgery, based on the data presented by the speaker?
- What does neuromorphic mean, based on the data presented by the speaker?
- What's about the implantable retina presented by the speaker?
- What are the key points of the artificial antibodies presented by the speaker?

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